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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,700	02/27/2002	Todd W. Seeley	PP-01406.004 / 200130.438	1172

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,700	SEELEY, TODD W.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6 and 16-48* is/are pending in the application.

4a) Of the above claim(s) *5,6,16-41,47 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *02-2702*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response filed on 09/03/03 has been acknowledged.
Claims 4, 42-46 are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). The fax phone numbers for the organization where this application or proceeding is assigned is ***703-872-9306****.*

Election/Restrictions

Applicant's election with traverse of Group I claims 4, 42-46 in Paper No. 09/03/03 is acknowledged. The traversal is on the ground(s) that there is no undue search burden to examine all the groups as single invention. This is not found persuasive because inventions of groups I-VII are distinct and are of separate use for the same reasons of record as set forth in the office action mailed on 07/29/03. In addition there exists search burden to examine all the groups as one single invention. For example searching the amino acid sequences of group I is not required for invention of group II, which requires searching an antibody. Thus these inventions are independent and distinct.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-6, 16-41 and 47-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 090303.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses any variant of huBUB3 protein which has 90% identity to a nucleic acid sequence which encodes the amino acid sequences of SEQ ID NO:2. The scope of invention as claimed also encompasses a variant of SEQ ID NO:2 which 95% identical to amino acid sequences of SEQ ID NO:2. The scope of invention as claimed encompasses an epitope bearing portion of the polypeptide of SEQ ID NO:2, wherein in the epitope comprises about 8-25 contiguous amino acid sequences of SEQ ID NO:2. In addition the scope of invention as claimed encompasses a huBUB3 fusion protein which comprises at least 8 contiguous amino acids of huBUB3 protein as shown in SEQ ID NO:2.

At best the specification only disclosed the amino acid sequences of SEQ ID NO:2 (huBUB3). The specification as filed fails to disclose any variant of huBUB3 polypeptide that has huBUB3 like activity explicitly or implicitly as putatively claimed

herein. In addition the specification fails to define any epitope-bearing portion found in the polypeptide of SEQ ID NO:2. Similarly the specification fails to define a fusion protein that consists of at least 8 contiguous amino acids huBUB3 protein as shown in SEQ ID NO:2.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only amino acid sequence of SEQ ID NO:2 which encodes HuBUB3 protein. The specification fails define any variant or epitope-bearing portion of huBUB3 protein. The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others

except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the polypeptide variants (as claimed) has been defined only by a statement of function that broadly encompasses a huBUB3 like protein activity or an antibody binding portion of huBUB3 protein (epitope), which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The state of the art at the time of filing was such that defining epitopes is not as easy as it seems. Even when the epitope is defined in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (see Greenspan et al, Nature Biotechnology 7:936-937, 1999). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 4, 42-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a an isolated huBUB3 polypeptide comprising the amino acid sequences of SEQ ID NO:2, does not reasonably provide enablement for

any variant or an epitope bearing portion of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Nature of Invention: Invention relates to variants and epitopes of huBUB3 protein.

Breadth of Claims and Guidance Provided in the Specification: The scope of invention as claimed encompasses any variant of huBUB3 protein which has 90% identity to a nucleic acid sequence which encodes the amino acid sequences of SEQ ID NO:2. the scope of invention as claimed also encompasses a variant of SEQ ID NO:2 which 95% identical to amino acid sequences of SEQ ID NO:2. The scope of invention as claimed encompasses an epitope bearing portion of the polypeptide of SEQ ID NO:2, wherein in the epitope comprises about 8-25 contiguous amino acid sequences of SEQ ID NO:2. In addition the scope of invention as calimed encompasses a huBUB3 fusion protein which comprises at least 8 contiguous amino acids of huBUB3 protein as shown in SEQ ID NO:2. At best the specification only disclosed the amino acid sequences of SEQ ID NO:2 (huBUB3). The specification as filed fails to disclose any variant of huBUB3 polypeptide that has huBUB3 like activity explicitly or implicitly as putatively claimed herein. In addition the specification fails to define any epitope-bearing portion found in the polypeptide of SEQ ID NO:2. Similarly the specification fails to define a fusion protein that consists of at least 8 contiguous amino acids huBUB3 protein as shown in SEQ ID NO:2.

State of Art and Predictability: The art at the time of filing define epitopes as a region on an antigen molecule to which antibody or the T cell receptor binds specifically. Antibodies binds in a more or less exact three-dimensional fit within an epitope. This structure may be formed from residues on different regions of protein antigen molecules, which in the native state are closely apposed due to protein folding. Thus the 3-dimensional structure of the protein molecule is considered essential. Epitopes recognized by T cells are peptide fragments processed by APCs. Since a continuous primary sequence is necessary for T cell recognition but not for antibody recognition, the epitopes recognized on the same protein molecule by each (antibody or T-cell) are different. In this regard, the specification fails to provide sufficient guidance and objective evidence as to the linear or three-dimensional conformation of the huBUB polypeptide, which may or may not constitute an epitope (see Herbert et al. The Dictionary of Immunology, Academic Press, 4th edition, 1995). Moreover, defining epitopes is not as easy as it seems. Even when the epitope is defined in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (Greenspan et al, Nature Biotechnology 7:936-937 (1999) see page 937, 2 column). Furthermore 5-10% variation (90-95% identical) as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the

ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976).

Undue experimentation: The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). In instant case screening of any and all natural and non-natural variants, wherein at least 5-10% amino acid are added substituted and /or deleted in the disclosed SEQ ID NO:2 is not considered routine. Making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein at least 5-10% amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants or epitopes that meet the requirements for the huBUB3 function. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of

enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed, since the applicant has not presented enablement commensurate in scope with the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838 (**571-272-0769**). The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be reached on 703-305-1998 (**571-272-0781**). The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
Patent examiner

JEFFREY FREDMAN
PRIMARY EXAMINER